Complete Summary

GUIDELINE TITLE

Recommendations for the use of cardiac markers in coronary artery diseases.

BIBLIOGRAPHIC SOURCE(S)

Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999 Jul;45(7):1104-21. [119 references] PubMed

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Chest pain
- Coronary artery diseases

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Cardiology
Critical Care
Emergency Medicine
Pathology

INTENDED USERS

Clinical Laboratory Personnel
Physicians

GUIDELINE OBJECTIVE(S)

To provide education and guidance in the use of cardiac markers

TARGET POPULATION

Patients with chest pain or coronary artery diseases

INTERVENTIONS AND PRACTICES CONSIDERED

Cardiac Markers

1. Cardiac troponin T or I (definitive marker)
2. CK-MB (early marker)
3. Myoglobin (early marker)

Note: Lactate dehydrogenase (LDH) and its isoenzymes are not recommended

Testing Methodology

1. Automated, continuous, random access immunoassay
2. Electrophoresis
3. Point-of-care (POC) testing

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Sixth Conference on the "Standards of Laboratory Practice", sponsored by the National Academy of Clinical Biochemistry (NACB), was held on August 4-5, 1998, at the Annual Meeting of the American Association of Clinical Chemistry, in Chicago, IL. An expert committee was assembled to write recommendations on the use of cardiac markers in coronary artery diseases. The NACB Committee prepared a preliminary draft of the guidelines, made them available on the World Wide Web (www.nacb.org), and distributed them before the presentations. The recommendations were revised and subsequently re-presented in part at the "Biomarkers in Acute Cardiac Syndromes Conference", sponsored by the Jewish Hospital Heart and Lung Institute, Louisville, KY, on October 16-17, 1998.

Approximately 100 individuals responded to various versions of these recommendations via direct correspondence, telephone calls to Committee members, electronic mail correspondence to the Committee Chairman, or oral questions and comments raised during one of the two conference presentations. Some of the recommendations were changed to reflect the consensus opinion. In cases in which there was no consensus, the Committee included pertinent discussion without necessarily changing the original recommendations. At times, the Committee members felt that although a particular recommendation might not be the current standard of care today, they anticipate that it likely will be adopted in the near future.

Listed with each recommendation is the degree of evidence from the literature and/or agreement from the consensus of participants who attended either presentation.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

This scheme is a modified version of the one defined by the American College of Cardiology (ACC)/American Heart Association (AHA):

Class I recommendation - one for which there is evidence and/or general agreement.

Class II recommendation - one for which there is conflicting evidence and/or a divergence of opinion about its usefulness/efficacy, but where the weight of evidence/opinion is in its favor.

Class III recommendation - one for which there is evidence and/or general agreement that a procedure is not useful or effective.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Names of the individuals who reviewed drafts of the guideline document are provided in Appendix 1 of the original guideline document.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Each recommendation is rated based upon the grade of the recommendation (Class I, Class II, Class III) as defined at the end of the Major Recommendations field.

<u>Recommendations for Markers in the Triage of Patients with Chest Pain</u>

Recommendation 1: Members of emergency departments, divisions of cardiology, hospital administrations, and clinical laboratories should work collectively to develop an accelerated protocol for the use of biochemical markers in the evaluation of patients with possible acute coronary syndromes (ACSs). Strength/consensus of recommendation: Class I.

For simplicity, this protocol should apply to either the facilitated diagnosis or the rule-out of acute myocardial infarction (AMI) in the emergency department (ED) or to routine diagnosis from other areas of the hospital, should a patient develop symptoms consistent with acute coronary syndromes while hospitalized. Strength/consensus of recommendation: Class II.

Recommendation 2: For routine clinical practice, blood collections should be referenced relative to the time of presentation to the ED and (when available) the reported time of chest pain onset. Strength/consensus of recommendation: Class I.

Recommendation 3: Two biochemical markers should be used for routine acute myocardial infarction (AMI) diagnosis: an early marker (reliably increased in blood within 6 h after onset of symptoms) and a definitive marker (increased in blood after 6-9 h, but has high sensitivity and specificity for myocardial injury, remaining abnormal for several days after onset). Strength/consensus of recommendation: Class II.

Recommendation 4: In patients with a diagnostic electrocardiogram (ECG) on presentation (ST-segment elevations, presence of Q waves or left bundle branch block in two or more contiguous leads), the diagnosis of AMI can be made and acute treatment initiated without results of acute cardiac marker testing. Strength/consensus of recommendation: Class I.

In AMI patients with diagnostic ECGs, biochemical marker testing at a reduced frequency of blood collection (e.g., twice a day) is valuable for confirmation of diagnosis, to qualitatively estimate the size of the infarction, and to detect the presence of complications such as a reinfarction. Strength/consensus of recommendation: Class I.

Recommendation 5: For detection of AMI by enzyme or protein markers, in the absence of definitive ECGs, the following sampling frequency is recommended:

Marker	Admission	2 to 4 hours	6 to 9 hours	12 to 24 hours
Early (< 6 hours)	X	X	X	(X)
Late (> 6 hours)	X	X	X	(X)

(X) indicates optional determinations.

Strength/consensus of recommendation: Class II.

Recommendation 6: For those emergency departments in which patient triage decisions are not made within the first few hours after emergency department presentation, the use of an early marker such as myoglobin may be unnecessary. In this case, only one definitive marker such as cardiac troponin is needed. The frequency of blood collection should also be reduced. Strength/consensus of recommendation: Class I.

Recommendations for Markers in Acute Coronary Syndromes

Recommendation 1: Two decision limits are needed for the optimum use of sensitive and specific cardiac markers such as cardiac troponin T and I (cTnT or cTnI). A low abnormal value establishes the first presence of true myocardial injury, and a higher value is suggestive of injury to the extent that it qualifies as

AMI, as defined previously by the World Health Organization (WHO) (World Health Organization, 1979). Strength/consensus of recommendation: Class II.

Recommendation 2: Chest pain patients with laboratory results for cTnT and cTnI between the upper limit of the reference interval and the decision limit for AMI should be labeled as having "myocardial injury." These patients should be admitted and acutely treated to reduce the risks associated with this injury (Hamm et al., 1998; Lindhal, Venge, & Wallentin, 1997). Strength/consensus of recommendation: Class I.

Recommendation 3: The World Health Organization (WHO) definition of AMI should be expanded to include the use of serial biochemical markers and not be limited to enzyme changes. It should be emphasized that rule-out of AMI cannot be made on the basis of data from a single blood collection. However, when very specific cardiac markers are used, the presence of an abnormal concentration from a single specimen can be highly diagnostic of myocardial injury. Strength/consensus of recommendation: Class I.

Recommendation 4: At this time (the time the guideline was written), there are no data available to recommend use of cardiac markers such as cTnT or cTnI for screening asymptomatic patients for the presence of acute coronary syndromes. The likelihood of detecting silent ischemia is extremely low and cannot justify the costs of screening programs. Additionally, there is no evidence that cardiac marker analysis of blood following stress testing can indicate the presence of coronary artery disease. Strength/consensus of recommendation: Class III (for use of cardiac markers for screening).

<u>Recommendations for Markers in Clinical Applications Other than AMI and Research</u>

Recommendation 1: For assessment of reperfusion status following thrombolytic therapy, at least two blood samples are collected and marker concentrations compared: time = 0, defined as just before initiation of therapy, and time = 1, defined as 90 min after the start. From these values, the determination of the (a) slope value ($marker_{t = 90}$ minus $marker_{t = 0}$)/90 min); (b) absolute value of $marker_{t = 90,}$ in minutes; or (c) the ratio of $marker_{t = 90}$/$marker_{t = 0}$ can be used as the discriminating factor between successful and unsuccessful reperfusion. However, monitoring with biochemical marker strategies has not been successful in distinguishing between thrombolysis in myocardial infarction (TIMI) grade 3 and TIMI grade 2 flow patients, rendering the utility of these measurements clinically problematic for determining complete reperfusion. Strength/consensus of recommendation: Class II.

Recommendation 2: Cardiac troponin T or I should be used for the detection of perioperative AMI in patients undergoing noncardiac surgical procedures. The same AMI decision limit should be used. Strength/consensus of recommendation: Class I.

Recommendation 3: Cardiac markers should not be routinely used for infarct sizing because the existing markers are inaccurate in the presence of spontaneous, pharmacologic, or surgical reperfusion. Strength/consensus of recommendation: Class III (for use of markers in infarct sizing).

Recommendation 4: Early in the process, manufacturers should seek assistance and provide support to professional organizations such as the American Association for Clinical Chemistry (AACC) or International Federation of Clinical Chemistry (IFCC) to develop committees for the standardization of new analytes. These organizations will determine the need for analyte standardization based on the potential clinical importance of the marker and gather the necessary scientific expertise for the formation of a standardization committee. Strength/consensus of recommendation: Class I.

Recommendation 5: Reference ranges are established for each marker on a population of normal healthy individuals using the 97.5 percentile (one-tail) of results. Separate cutoff concentrations for results indicative of AMI are also necessary for all cardiac markers. Standardized receiver operating characteristic (ROC) curves should be used to establish AMI decision limits, using carefully selected and diagnosed patient populations. Strength/consensus of recommendation: Class I.

Recommendation 6: For research studies involving the kinetics of release and appearance of new biochemical markers, the time course of release and appearance in blood must be defined relative to the onset of clinical symptoms. Strength/consensus of recommendation: Class I.

The diagnostic accuracy of these new markers may be compromised if the diagnosis of AMI for study patients is based on standard enzyme markers that themselves have sensitivity and/or specificity limitations (e.g., total CK and CK-MB). Therefore, AMI diagnosis should be defined by WHO criteria, but with the substitution of "unequivocal serial changes of cTnT or cTnI" as the principal biochemical marker, in place of the current WHO criteria of "unequivocal serial enzyme changes." Strength/consensus of recommendation: Class II.

<u>Recommendations for Assay Platforms and Markers of Acute Myocardial Infarction</u>

Recommendation 1: Cardiac troponin (T or I) is the new standard for diagnosis of myocardial infarction and detection of myocardial cell damage, replacing CK-MB. Strength/consensus of recommendation: Class II.

There is no longer a role for lactate dehydrogenase and its isoenzymes in the diagnosis of cardiac diseases. Strength/consensus of recommendation: Class I.

Recommendation 2: The laboratory should perform stat cardiac marker testing on a continuous random-access basis, with a target turnaround time (TAT) of 1 h or less. The TAT is defined as the time from blood collection to the reporting of results. Strength/consensus of recommendation: Class II.

Recommendation 3: Institutions that cannot consistently deliver cardiac marker turnaround times of approximately 1 h should implement point-of-care (POC) testing devices. The cutoff concentrations of these devices should be set at the 97.5% upper reference limits so that the devices can detect the first presence of true myocardial injury. Strength/consensus of recommendation: Class I.

Recommendation 4: Among other tasks, laboratory personnel must be involved in the selection of devices, the training of individuals to perform the analysis, the maintenance of POC equipment, the verification of the proficiency of operators on a regular basis, and the compliance of documentation with requirements by regulatory agencies such as the Health Care Finance Administration and the Clinical Laboratory Improvement Act of 1988. In meeting these requirements, quality-assurance and quality-control programs must be instituted and fully documented on a regular basis. Strength/consensus of recommendation: Class I.

Recommendation 5: Assays for cardiac markers should have an imprecision (CV) $\leq$10% at the AMI decision limits and an assay turnaround time of <30 min. Before launch, assays must be characterized with respect to potentially interfering substances (e.g., other related proteins, human anti-mouse antibodies [Fitzmaurice et al., 1998; Kricka et al., 1990] and other interferences). Strength/consensus of recommendation: Class II.

Recommendation 6: Plasma or anticoagulated whole blood are the specimens of choice for the stat analysis of cardiac markers. Strength/consensus of recommendation: Class I.

Definitions:

This scheme is a modified version of the one defined by the American College of Cardiology (ACC)/American Heart Association (AHA):

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Class III recommendation - one for which there is evidence and/or general agreement that a procedure is not useful or effective.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting each recommendation is discussed in the guideline document after each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of cardiac markers in patients with chest pain and coronary artery diseases for early detection of myocardial injury

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Although entitled "Standards of Laboratory Practice", the statements made in this document are "recommendations" and not practice standards. These recommendations represent the individual experiences of experts in the field of clinical biochemistry, cardiology, and emergency medicine, and should be examined for appropriateness in individual or unique settings.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999

GUIDELINE DEVELOPER(S)

National Academy of Clinical Biochemistry - Professional Association

SOURCE(S) OF FUNDING

National Academy of Clinical Biochemistry

GUIDELINE COMMITTEE

National Academy of Clinical Biochemistry Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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*Participated in discussion of recommendations as members of the International Federation of Clinical Chemistry Committee for Standardization of Markers of Cardiac Damage

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Academy of Clinical Biochemistry (NACB) Web site:

- Word Format

- Portable Document Format (PDF)

Print copies: National Academy of Clinical Biochemistry publications are available through American Association for Clinical Chemistry (AACC) Press. To make a purchase or request a catalog, contact AACC Customer Service at 202-857-0717 or custserv@aacc.org.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 10, 2003. The information was verified by the guideline developer on June 5, 2003.

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